Intra-Cellular Therapies Highlights Lumateperone Presentations at the 58th Annual Meeting of the American College of Neuropsychopharmacology

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Bipolar depression: Study 404, A Phase 3 Clinical Trial of lumateperone for the treatment of Bipolar Depression, investigating the potential of lumateperone as a new option for the treatment of depressive episodes in patients suffering from Bipolar I or Bipolar II disorder.

Schizophrenia: Lumateperone's clinical profile including its motor and cardiometabolic profile was showcased in pooled analyses of randomized short-term clinical trials and a long-term safety study.

Lumateperone and the Metabolic Syndrome (MetSy): Post-hoc analyses from short-term placebo-controlled studies in schizophrenia on MetSy in patients treated with lumateperone and in patients treated with risperidone were presented.

NEW YORK, Dec. 12, 2019 (GLOBE NEWSWIRE) -- Intra-Cellular Therapies, Inc. (Nasdaq:ITCI), a biopharmaceutical company focused on the development of therapeutics for central nervous system (CNS) disorders, today announced data featured yesterday during the 58th Annual Meeting of the American College of Neuropsychopharmacology (ACNP) held in Orlando, FL, December 8-11, 2019 included:

- *"Lumateperone (ITI-007) in the Treatment of Bipolar Depression: Results from a Randomized Clinical Trial" (Poster W123)*

This poster presented data from the positive Phase 3 clinical trial of lumateperone for the treatment of patients with bipolar depression (ITI-007-404 or Study '404). Study 404 was conducted globally, including in the U.S., and included 381 patients randomized (1:1) to receive lumateperone 42 mg or placebo once daily for six weeks. Lumateperone met its primary endpoint of change from baseline at Week 6 on the Montgomery-Åsberg Depression Rating Scale (MADRS) total score versus placebo ($p<0.0001$; effect size (ES) = 0.56). In the intent-to-treat study population, the LS mean improvement from baseline for lumateperone 42 mg was 16.7 points, versus 12.1 points for placebo, for a 4.6-point difference between the two groups. Lumateperone also met the study's key secondary endpoint, Clinical Global Impression Scale for Bipolar for Severity of Illness (CGI-BP-S) Total Score ($p<0.001$; ES = 0.46). In addition, the CGI component that specifically assesses depression showed improvement with lumateperone versus placebo (CGI-BP-S Depression Score; $p<0.001$; ES = 0.50). This improvement was statistically significant as early as week 1, the first time point measured, and was maintained at every time point throughout the study.

In subgroup analyses of both Bipolar I patients and Bipolar II patients, statistically significant improvements were seen versus placebo on the MADRS total score (Bipolar I patients: $p<.0001$; ES: 0.49; and Bipolar II patients: $p<.001$; ES: 0.81).

These results were supported by statistically significant improvements on responder rates and remission rates, demonstrating the clinical meaningfulness of the primary outcome, with 51.1% of patients on lumateperone meeting MADRS response criteria (50% improvement from baseline) versus 36.7% for placebo at Day 43 ($p<0.001$). Additionally, 39.9% of patients on lumateperone were considered remitters (MADRS ≤12) versus 33.5% for placebo ($p=<0.05$).

The safety profile in this study was consistent with previously reported placebo-controlled and open-label studies in patients with schizophrenia. Lumateperone showed similar effects as placebo on assessments of body weight, metabolic parameters, extrapyramidal symptoms, and prolactin. Rates of akathisia, restlessness and extrapyramidal symptoms combined were less than 1% and similar to placebo. The most commonly reported adverse events that were observed at a rate greater than 5% and higher than placebo were somnolence (8.5%) and nausea (6.4%). The rates of discontinuation due to treatment emergent adverse events for lumateperone were less than 5 percent.

"The results of this trial including lumateperone's separation from placebo on multiple measures of depression accompanied by its metabolic and motor profile are impressive," said Joseph Calabrese, MD, Director, Mood Disorders Program, Department of Psychiatry, University Hospitals Cleveland Medical Center. "Lumateperone represents a potential important option for the treatment of patients suffering from Bipolar I and Bipolar II disorder who are experiencing depressive episodes. These are highly prevalent and difficult to treat conditions for which there is a need for effective and better tolerated options."

- *"Efficacy and Safety of Lumateperone 42 mg in the Treatment of Schizophrenia: A Pooled Analysis of Randomized Clinical Trials" (Poster W201)*

This poster highlighted the clinical results of lumateperone 42 mg, including its safety and tolerability profile from the short-term controlled studies of lumateperone in the treatment of patients with acute exacerbations of schizophrenia. The poster included additional post-hoc pooled analyses that found lower rates of MetSy in patients treated with lumateperone than in patients treated with risperidone.

In these double-blind, placebo-controlled studies of 4 to 6 weeks duration, patients were randomized to either lumateperone 42mg (n=406), risperidone 4mg (n=255) or placebo (n=412). The percentage of patients meeting criteria for MetSy at baseline was similar across groups (18.2% for lumateperone, 19.2% for risperidone and 17.0% for placebo).

At study endpoint, fewer patients on lumateperone met the MetSy criteria compared with the percentage on risperidone (15.0% v. 24.7%). Among those patients with MetSy at baseline, the percentage who no longer met criteria for MetSy after study treatment was nearly twice as high among patients treated with lumateperone as among patients treated with risperidone (45.9% v. 24.5%). Among patients without MetSy at baseline, the percentage that developed MetSy during study treatment with lumateperone was half that in risperidone-treated patients (6.3% v. 12.6%).

"Metabolic Syndrome is a highly prevalent set of risk factors among patients with schizophrenia and is associated with many commonly prescribed antipsychotics," said Dr. Christoph Correll, Professor of Psychiatry and Molecular Medicine at the Zucker School of Medicine at Hofstra/Northwell, New York. "Previous data have indicated that lumateperone is associated with effects similar to placebo in short-term trials on body weight and cardiometabolic parameters, including levels of blood glucose, insulin, and cholesterol. Moreover, in a switch safety study, lumateperone was associated with improvements in several important cardiometabolic parameters. These new safety analyses in the broader context of a well-recognized clinical entity, the Metabolic Syndrome, which is a well-established marker for overall cardiovascular risk, are encouraging."

- *"Additional Results from a 12-Month Open-Label Safety Study of Lumateperone (ITI-007) in Patients with Stable Symptoms of Schizophrenia" (Poster W203).*

Additional results from the lumateperone long-term safety study were presented. The data presented showed the safety of long-term lumateperone treatment was consistent with previously reported studies and associated with a low risk of metabolic, EPS, and prolactin side effects. Patients with stable schizophrenia symptoms continued to show improvement in PANSS scores with lumateperone treatment throughout the 1-year open-label study. Furthermore, in patients with schizophrenia and comorbid depression symptoms at baseline lumateperone 42 mg improved depressive symptoms.

About Lumateperone Bipolar Depression Program

The lumateperone clinical trial program in bipolar depression includes three Phase 3 trials. Two trials, Study 401 and Study 404, evaluated lumateperone as monotherapy and the third trial, Study 402, is evaluating lumateperone as an adjunctive therapy to lithium or valproate. The safety and efficacy of lumateperone in bipolar disorder has not been established.

About Metabolic Syndrome (MetSy)

According to the National Heart, Lung, and Blood Institute, MetSy is defined as the presence of at least 3 of the following 5 risk factors: abdominal obesity as measured by waist circumference; elevated triglyceride levels; low HDL cholesterol levels; high blood pressure; and elevated fasting blood sugar. People who meet this definition have 5-6 times the risk of developing type 2 diabetes and a 3-6 times increased risk of mortality due to coronary heart disease than people who do not[1]. People with severe mental illness have significantly higher rates of the MetSy than the general population[2] and are likely to die 12-15 years earlier, with cardiovascular disease as the primary driver for this early mortality[3]. A major factor in the development of MetSy among people with severe mental illness is the use of antipsychotic medication[4].

References

1. Alberti K, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120(16):1640-1645
2. Vancampfort D, Stubbs B, Mitchell AJ, De Hert M, Wampers M, Ward PB, Rosenbaum S, Correll CU. Risk of metabolic syndrome and its components in people with schizophrenia and related psychotic disorders, bipolar disorder and major depressive disorder: a systematic review and meta-analysis. World Psychiatry 2015;14(3):339-47.
3. Correll CU, Solmi M, Veronese N, et al. Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls. World Psychiatry 2017;16(2):163-180
4. De Hert M, Detraux J, van Winkel R, Yu W, Correll CU. Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. Nat Rev Endocrinol 2011;8(2):114-26.

About Lumateperone

Lumateperone is an investigational molecule that provides selective and simultaneous modulation of serotonin, dopamine, and glutamate - three neurotransmitter pathways implicated in severe mental illness. Lumateperone is a potent serotonin 5-HT2A receptor antagonist, a dopamine receptor phosphoprotein modulator (DPPM) acting as a presynaptic partial agonist and postsynaptic antagonist at dopamine D2 receptors, a dopamine D1 receptor-dependent indirect modulator of glutamate (both NDMA and AMPA), and a serotonin reuptake inhibitor. Lumateperone in an investigational new drug under review with the FDA for the treatment of schizophrenia, its safety and efficacy has not been established, and it has not been approved for marketing for any use by the U.S. Food and Drug Administration (FDA) or any other regulatory authority in any other jurisdiction.

About Intra-Cellular Therapies

Intra-Cellular Therapies is developing novel drugs for the treatment of neuropsychiatric and neurodegenerative diseases and diseases of the elderly, including Parkinson's and Alzheimer's disease. The Company is developing its lead drug candidate, lumateperone (also known as ITI-007), for the treatment of schizophrenia, bipolar disorder, behavioral disturbances in patients with dementia, including Alzheimer's disease, depression and other neuropsychiatric and neurological disorders. Lumateperone is under review by the FDA for the treatment of schizophrenia and is in Phase 3 clinical development for the treatment of bipolar depression. Intra-Cellular Therapies is also utilizing its phosphodiesterase (PDE) platform and other proprietary chemistry platforms to develop drugs for the treatment of CNS and other disorders. The lead molecule in the Company's PDE1 portfolio, ITI-214, is in development for the treatment of symptoms associated with Parkinson's disease and for the treatment of heart failure.

Forward-Looking Statements

This news release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 that involve risks and uncertainties that could cause actual results to be materially different from historical results or from any future results expressed or implied by such forward-looking statements. Such forward-looking statements include statements regarding, among other things, the safety and efficacy of our product candidates; the potential benefits and uses of our product candidates and development efforts and plans under the caption "About Intra-Cellular Therapies." All such forward-looking statements are based on management's present expectations and are subject to certain factors, risks and uncertainties that may cause actual results, outcome of events, timing and performance to differ materially from those expressed or implied by such statements. These risks and uncertainties include but are not limited to the following: whether the NDA for lumateperone for the treatment of schizophrenia will be approved by the FDA and whether the FDA will complete its review within the target timelines including the new PDUFA goal date; whether, during its review of our applications for regulatory approval of our product candidates, we will be able to provide in a timely manner all information requested by the FDA and whether the FDA will determine information we submit in the course of such reviews is satisfactory; risks associated with our current and planned clinical trials; we may encounter unexpected safety or tolerability issues with lumateperone in ongoing or

future trials and other development activities; our other product candidates may not be successful or may take longer and be more costly than anticipated; product candidates that appeared promising in earlier research and clinical trials may not demonstrate safety and/or efficacy in larger-scale or later clinical trials; our proposals with respect to the regulatory path for our product candidates may not be acceptable to the FDA; our reliance on collaborative partners and other third parties for development of our product candidates; and the other risk factors detailed in our public filings with the Securities and Exchange Commission. All statements contained in this press release are made only as of the date of this press release, and we do not intend to update this information unless required by law.

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